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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/728,420	11/28/2000	Steven K. Yoshinaga	A-579C	7508

7590 07/14/2003

M. Paul Baker
Finnegan ,Henderson , Farabow , Garrett
1300 I Street N.W.
Washington, DC 20005-3315

EXAMINER
ROARK, JESSICA H

ART UNIT	PAPER NUMBER
1644	23

DATE MAILED: 07/14/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/728,420	Applicant(s) YOSHINAGA ET AL.	
	Examiner Jessica H. Roark	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 April 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-55* is/are pending in the application.

4a) Of the above claim(s) *1-7,9,11,13-18 and 24-42* is/are withdrawn from consideration.

5)☒ Claim(s) *50, 51 and 55* is/are allowed.

6)☒ Claim(s) *8,10,12,19-23,43-49 and 52-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 October 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *20* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 4/30/03 (Paper No. 22), is acknowledged.
Claims 43-55 have been added.
Claims 8, 10, 12, 19-20 and 22 have been amended.
Claims 1-55 are pending.

Claims 1-7, 9, 11, 13-18 and 24-42 in full, *and claims 8 and 19-23 as they read on the non-elected CRP-1 polypeptide of SEQ ID NO:2 encoded by SEQ ID NO:1,* are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 15 based upon an incomplete response.

It is noted that Applicant has amended instant claims 8 and 19-23 to now recite subject matter of Group III (as set forth in Paper No. 13), a group non-elected without traverse in Paper No. 15.

Claims 10, 12, and 43-55 (in full) and claims 8 and 19-23 only as they relate to a B7RP1 polypeptide (SEQ ID NOS:7, 12 and 17, encoded by SEQ ID NOS:6, 11 and 16, respectively) *are under consideration in the instant application.*

2. This Office Action will be in response to applicant's arguments, filed 4/30/03 (Paper No. 22).
The rejections of record can be found in the previous Office Action (Paper No. 18).

It is noted that New Grounds of Rejection are set forth herein.

Rejection and objections of record in Paper No. 18 but not reiterated herein have been obviated by Applicant's amendment, filed 4/30/03.

Claim Rejections - 35 USC § 112 second paragraph

3. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 8, 10, 12, 19-23, 43-49, 52-54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 8, 10, 12, 46-49 and claims dependent thereon are indefinite in that they recite an arbitrary protein name, "B7RP1". The specification does not appear to provide an explicit definition of the term "B7RP1" since "all related polypeptides described herein", including polypeptides which do necessarily share substantial structure or function with the polypeptides set forth in SEQ ID NOS:7 or 12, are encompassed in the description of a "B7RP1 polypeptide" disclosed on pages 41-42 of the specification.

Applicant should particularly point out and distinctly claim "B7RP1" by claiming a sufficient number of characteristics associated with the protein (e.g. activity and amino acid composition, etc.).

B) Claims 8, 10, 12, 46-49 and claims dependent thereon are indefinite in their recitation of polypeptides and polypeptide fragments having "at least one activity characteristic" of B7RP1. Although the specification discloses on page 43 at lines 12-23 that binding to a CRP1 polypeptide and the ability to stimulate T cell proliferation and/or activation are activities which are characteristic of a B7RP1 polypeptide, the disclosure of two activities possessed by a B7RP1 polypeptide does not establish the metes and bound of what constitutes an "activity characteristic" of B7RP1.

It is suggested that Applicant limit the claims to a disclosed activity, but Applicant is cautioned that recitation of the term "CRP1", an arbitrary protein name, would be considered indefinite as set forth supra for the term "B7RP1".

C) The recitation of "high stringency conditions" in claims 8, 10, 12 and 54 (as well as claims dependent thereon) is ambiguous. Although the specification discloses on page 25 general parameters for calculating such conditions and examples of such conditions, in the absence of a clear definition of the metes and bounds of this phrase it is unclear which conditions are actually claimed.

It is suggested that Applicant amend the claims to recite a particular set of hybridization and wash conditions, such as those exemplified on page 25 of the specification, to overcome this rejection.

D) Applicant is reminded that any amendment must point to a basis in the specification so as not to add new matter. See MPEP 714.02 and 2163.06.

Claim Rejections - 35 USC § 112 first paragraph

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 8, 10, 12, 19-23, 45-47 and 53-54 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The following *written description* rejection is set forth herein.

The specification discloses that the polypeptides of SEQ ID NO:12 and SEQ ID NO:17 are two forms of a human B7-RP1 polypeptide; and that SEQ ID NO:7 is a mouse B7-RP1 polypeptide.

Applicant's arguments, filed 4/30/03, with respect to the amended claims have been fully considered but have not been found convincing. Applicant's arguments are addressed below in the context of the reiteration of the rejection of record in Paper No. 18 as applied to the amended and newly added claims.

The amended and newly added claims recite:

A) "variant" language, and

B) polypeptides comprising "fragments".

The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 3rd column).

Regarding the instant claim limitations, the specification does not appear to provide an adequate written description for the following reasons:

A) "Variants":

In view of Applicant's comments filed 4/30/03 regarding the inaccuracy of saying that the "derivative" as recited in claim 20 is also a "variant", it is first noted that although the specification does distinguish "derivatives" (page 43 at lines 1-11) from "variants" (page 42 at lines 25-36); both the specification at these locations and the claims in view of their dependency indicate that a variant polypeptide is a polypeptide of the invention from which a derivative can be produced by the chemical modification. Thus the term "variant" does include "derivatives", as recited in instant claim 20.

As previously noted, Applicant has disclosed two human and one mouse B7-RP1 polypeptide, and thus has disclosed only a limited number of "variants". The claims recite a genus of polypeptides but do not require that the instant polypeptides share any testable functional activity, a feature deemed essential to the instant invention. In the absence of a particular testable function and some structural basis for that function that must be maintained by the members of the genus, the claimed invention is not described in such a way as to reasonably convey to one of ordinary skill in the art that the inventor, at the time the application was filed, had possession of the invention. See Regents of the University of California v. Eli Lilly & Co., 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Applicant argues in the response filed 4/30/03 with respect to what the Examiner has broadly characterized as "variant" language (i.e., percent identity or other variations in the polypeptide sequence) that functionality is not essential to the invention and that, even were it essential, the instant claims now recite a function (i.e., "at least one activity characteristic of B7RP1"). Applicant further argues that a recitation of "70% identity" provides adequate structure to describe the instantly claimed polypeptides.

However, there does not appear to be an adequate written description in the specification as filed as to a *correlation* between the structures encompassed by 70% identity or variants of the recited sequence and any *particular* function. Further, it is noted that the instant claims fail to provide a recitation of a meaningful function which could be correlated to a particular structure.

The Examiner acknowledges that a recitation of a particular function is not required for those polypeptides comprising a *defined* structure for which a function has been described in the specification. However, when the structure of the polypeptides in the genus varies in such a way that the aspect of the structure that provided the described function is no longer necessarily present, then a testable functional activity is essential to an adequate written description of the recited genus.

B) "Polypeptides Comprising Fragments":
As previously noted, fragment language that encompasses open (comprising) claim language permits unidentified flanking sequence to be added any subsequence of a particular SEQ ID NO and so does not allow one skilled in the art to visualize or recognize the identity of the subject matter purportedly described. Fragments which comprise unidentified flanking sequence or have variation within their sequence thus do not meet the written description requirement. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (id at 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (id at 1116.).

Applicant argues in the Remarks filed 4/30/03 that it is not necessary that every possible flanking sequence be described, and that "comprising" language in and of itself does not render a claim unpatentable. The Examiner acknowledges both points, but notes that this in order to meet the written description requirement there must be a structure conserved that is representative of the genus claimed. For example, comprising language is appropriate with respect to polypeptides comprising the full length coding sequence or comprising an internal fragment of a given polypeptide to which a particular function can be attributed.

However, when the fragment is not a functional fragment then the function of members of the genus of polypeptides comprising that fragment depends upon the flanking sequences and a description of the flanking sequence is required. In addition, it is noted that the instant claim language is not drawn to true internal fragments of B7RP1 having a minimal number of amino acid residues as recited (e.g., a fragment of SEQ ID NO:7 comprising at least about 50 amino acid residues"), but instead is drawn to polypeptides comprising these fragments and thus does not require that the flanking sequence be the same as those of the sequences flanking the fragment in SEQ ID NO:7.

In view of the large genus of polypeptides encompassed by the instant claim language and the absence of a correlation between a structures of each genus and a testable function shared by those structures which vary from the fully described polypeptide sequences; the Examiner maintains that the he specification fails to provide an adequate written description of the above noted claim limitations.

Applicant is again directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Alternatively, Applicant is invited to point to clear support or specific examples of the claimed invention in the specification as-filed.

The rejections of record are therefore maintained with respect to the amended and newly added claims.

7. Claims 8, 10, 12, 19-23, 45-47 and 53-54 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for

B7-RP1 polypeptides "consisting of" or "comprising" SEQ ID NO:7, 12 or 17;
B7-RP1 polypeptides encoded by nucleic acids "consisting of" or "comprising" SEQ ID NO:6, 11 or 16;
fragments of SEQ ID NO:7, 12 or 17 in which the claim language clearly limits the fragments to *sub*sequence of SEQ ID NO:7, 12 or 17;
"derivatives" which are clearly limited to chemical derivatives (e.g., as recited in claim 21);
fusion polypeptides defined as set forth above and fused to a heterologous amino acid sequence; and
polypeptides having only limited deviation from a reference sequence (e.g., a polypeptide 95% identical over the full length of SEQ ID NO:7) AND having a testable function supported in the specification as filed (and priority documents);

does not reasonably provide enablement for "variant" language or polypeptides comprising "fragments"; and does not reasonable provide enablement for the scope of activities "characteristic" of B7RP1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicant's arguments, filed 4/30/03, with respect to the amended claims have been fully considered but have not been found convincing. Applicant's arguments are addressed below in the context of the reiteration of the rejection of record in Paper No. 18 as applied to the amended and newly added claims.

The specification discloses that the polypeptides of SEQ ID NO:12 and SEQ ID NO:17 (encoded by SEQ ID NOS:11 and 16, respectively) are two forms of a human B7-RP1 polypeptide; and that SEQ ID NO:7 (encoded by SEQ ID NO:6) is a mouse B7-RP1 polypeptide. The specification also discloses (e.g., Example 8) on pages 81-83 that B7-RP1 is, along with CRP1, part of a costimulatory receptor-ligand pair.

In response to Applicant's Remarks filed 4/30/03, it is first noted that any polypeptide whose sequence differs from a reference sequence may be broadly construed to be a "variant" of that reference sequence. The Examiner chose to address claim language that recited polypeptides having changes in their amino acid, whether it be because the claim language encompassed chemical derivative of variants, a recitation of percent identity, or a polypeptide encoded by a hybridizing nucleic acid, because the issues with respect to these recitations are essentially the same: in each case the amino acid sequence differs from the reference sequence. "Allelic variants" and "splice variants" raise additional issues, and so were addressed separately in Paper No. 18.

As previously noted, the state of the art at the time the invention was made recognized that even single amino acid differences can result in drastically altered functions between two proteins. For example, Metzler et al. (Nature Structural Biol. 1997; 4:527-531, of record) showed that any of a variety of single amino acid changes can alter or abolish the ability of the CTLA4 to interact with its ligands CD80 and CD86 (B7-1 and B7-2) (e.g., summarized in Table 2). The variation in function among "B7-like" polypeptides is further emphasized by the teachings of Coyle et al. (Nature Immunol. 2:203-209 2001, of record) who show that the B7-like family members have distinct expression patterns *and distinct functions* , even though they share certain conserved amino acid residues and domain structure (see in particular Figures 2 and 3).

Thus the state of the art recognized that it is unpredictable if any particular functional activity will be shared by two polypeptides having less than 100% identity over the full length of their sequences.

Given the extensive variation permitted by the instant claim language drawn to polypeptides which vary in their amino acid sequence, the skilled artisan would not reasonably expect such "variant" polypeptides to have the same function as the instantly recited SEQ ID NOS, particularly when the family of B7-like proteins was known to have variable function.

The specification does not appear to provide sufficient guidance as to which residues should or should not be changed to preserve any particular function. Although the specification does provide working examples of human and mouse B7-RP1 polypeptides, the variation permitted by the instant claim language is extensive. Consequently, the experimentation left to those skilled in the art to determine which "variant" sequences would still result in polypeptides having the same function as a the human and mouse B7-RP1 polypeptides disclosed in the specification as filed is unnecessarily, and improperly, extensive and undue.

Applicant asserts in the Remarks filed 4/30/03 that because the instant claims now require that the polypeptide have at least one activity "characteristic of B7RP1", the skilled artisan would be able to make polypeptides having changes in their amino acid sequence and select for those which maintained at least one activity characteristic of B7RP1.

However, the specification as filed appears to provide sufficient guidance only with respect to two activities of B7RP1: binding to CRP1 and stimulation of T cell proliferation and/or activation (page 43 at lines 12-23). The instant recitation encompasses in its scope any activity that may, by any undefined criteria, be considered to be an "activity characteristic" of B7RP1. The state of the art at the time the invention was made did not recognize what those activities of B7RP1 were. In addition, as set forth supra, the skilled artisan at the time the invention was made recognized that polypeptides belonging to the B7 family of molecules had distinct functions. Thus the skilled artisan recognized that for any new member of the B7 family, it was unpredictable as to what particular activities would be "characteristic" of a given member. Further, it is unclear from the guidance provided in the specification as filed as to what constitutes a "characteristic" activity. Is an activity "characteristic" if other molecules in a family share that activity (e.g., other members of the B7 family stimulate T cells to proliferate)? In view of the limited number of working examples regarding activities of a B7RP1 polypeptide, the limited guidance as to what constitutes a "characteristic" activity, and the scope of activities encompassed; there does not appear to be sufficient guidance provided in the specification as filed with respect to an "activity characteristic of B7RP1".

Applicant also argues that it would not require undue experimentation to make polypeptides having 70% identity to one of the B7RP-1 polypeptides because it was routine practice in the art at the time the invention was made to make modifications in a polypeptide and test it for activity. Applicant equates the experimentation involved to that of making and screening monoclonal antibodies for a particular specificity. However, the instant fact pattern lacks the predictability associated with making and screening monoclonal antibodies. In the absence of guidance as to which amino acid residues provide a particular function, it is unpredictable which, if any, sequences having 70% identity would maintain that function. In the absence of such guidance, the claim is little more than a wish to know the identity of those related sequences which any function which may be considered an 'activity characteristic of B7RP1".

It is again suggested that Applicant limit the claims sequences having only limited variation (e.g. 95% identity) *over the full length* of the sequence, AND *possessing testable functional activity* supported in the specification and priority documents.

The instant claims also still recite in various forms polypeptides comprising "fragments" of a certain number of amino acid residues of the various SEQ ID NOS (or encoding nucleic acids). "Comprising" language opens the claim up to the inclusion of additional residues of undisclosed identity and number flanking the recited "fragment". It is again acknowledged that the skilled artisan can make fragments *limited* to *sub*sequences of the individual SEQ ID NOS without undue experimentation. However, before the skilled artisan can make polypeptides comprising "fragments" with additional flanking sequence, guidance is required with respect to the identity of those flanking sequences. In the instant case however, the specification does not appear to provided this needed guidance. Therefore the scope of the instant claims encompassing "fragments comprising" does not appear to be commensurate with the enablement provided by the instant disclosure.

Applicant argues in the Remarks filed 4/30/03 that the specification provides guidance as to flanking sequences that may be added to a fragment of B7RP1, such as the addition of the Fc region of IgG1, and asserts that other fusions of a B7RP1 fragment to other proteins could also be prepared.

The Examiner has acknowledged previously that the specification does provide sufficient guidance with respect to certain fusion proteins (see introductory statement of the rejection supra and in Paper No. 18). However, guidance with respect to a fusion protein comprising the extracellular domain fragment of B7RP1 and the Fc region of IgG1 is a single example limited to a particular fragment of B7RP1, the extracellular domain. The scope of the instant claims encompasses *any* fragment and *any* additional sequences. The issue is not the "comprising" language per se, it is the fact that insufficient guidance appears to have been provided with respect to the identity of the parts.

Thus with respect to the above noted claim limitations, each of which encompass considerable breadth and for each of which the specification provides only limited guidance; it would require undue experimentation of the skilled artisan to make and use such polypeptides; thus the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

The rejections of record are therefore maintained with respect to the amended and newly added claims.

8. Claim 49 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The following written description rejection is set forth herein. This is a New Matter rejection for the following reasons:

Applicant's amendment asserts that no New Matter has been added and points to the specification at page 43, lines 12-22 and Figure 12 for support for the newly added claim reciting "a carboxy terminus at about residue 302".

However, the specification does not appear to provide an adequate written description of "a carboxy terminus at about residue 302". Page 43 at lines 12-22 appears to be cited to support other aspects of claim 49. Figure 12 provides an amino acid sequence showing that amino acid 302 is the carboxy terminus. There does not appear to be a description either in Figure 12 or elsewhere in the specification or original claims that the Examiner was able to identify of variation in the carboxy terminus that could be construed as providing support for "at about residue 302". A single species of carboxy terminus within the scope of "at about residue 302" has been described.

It is acknowledged that there is support for alternate amino termini (as recited in instant claim 48) and that if the truncated amino terminus is renumbered as "1" then the polypeptide set forth in Figure 12A could be said to have a carboxy terminus at about residue 302. However, there does not appear to be sufficient support for the instant wording describing an *alternate* carboxy terminus since it is the length of the polypeptide that changes with an amino terminal truncation – not the identity of the residues found at he carboxy terminus.

The instant claims now recite limitations which were not clearly disclosed in the specification and claims as filed, and now change the scope of the instant disclosure as filed. Such limitations recited in the present claims, which did not appear in the specification or original claims, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the New Matter in the response to this Office Action.
Alternatively, Applicant is invited to clearly point out the written support for the instant limitations.

Claim Rejections – 35 U.S.C. §§ 102 and 103

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

10. Claims 8, 10, 12, 43, 45-47 and 52-54 are rejected under 35 U.S.C. 102(a) as being anticipated by Ishikawa et al (DNA Res. June 1998; 5:169-176, of record, see entire document) as evidenced by GenBank Accession No. AB014553 (released 06 Feb 1999, of record).

Applicant's arguments, filed 4/30/03, with respect to the amended claims have been fully considered but have not been found convincing. Applicant's arguments are addressed following a reiteration of the rejection of record in Paper No. 18 as applied to the amended and newly added claims.

Ishikawa et al. teach gene number KIAA0653, and that the sequence information for the cDNA and the protein product of KIAA0653 is available under accession number AB014553 (see entire document, but especially Table 1, first column). Ishikawa et al. also teach that the protein product of KIAA0653 was produced by in vitro translation (see comments in Section 2.1 on page 169 regarding original screening method) and that the 558 amino acid open reading frame encodes a protein of apparent molecular mass of 60 kDa (Table 1).

Ishikawa et al. teach that the KIAA0653 has homology to CD80, the original member of the B7 family of co-stimulatory proteins (e.g. see Table 2, page 175).

The protein product of KIAA0653 encompasses the entire amino acid sequence set forth in SEQ ID NO:12. Thus the protein product of KIAA0653 is a polypeptide comprising:

the amino acid sequence as set forth in SEQ ID NO:12;

the mature amino acid sequence as set forth in SEQ ID NO:12 comprising a mature amino terminus at any one of residues 19, 20, 21, 22, 24 or 28; and

a fragment of at least about 25, 50, 75, 100 or greater than 100 amino acid residues of instant SEQ ID NO: 12.

The protein product of KIAA0653 also encompasses the amino acid sequence as set forth in SEQ ID NO:17, except for the final 2 amino acids. Thus the protein product of KIAA0653 is also a polypeptide comprising a fragment of at least about 25, 50, 75, 100 or greater than 100 amino acid residues of instant SEQ ID NO: 17.

The protein product of KIAA0653 is a polypeptide encoded by a nucleic acid that includes the coding region of SEQ ID NO:11 and comprises a fragment of the nucleic acid sequence of SEQ ID NO:16.

Applicant argues in the Remarks filed 4/30/03 that Ishikawa et al. is a non-enabling reference because it does not by itself place the public in possession of the invention without the teachings of the evidentiary reference of GenBank Accession No. AB014553, which is not available as prior art.

It is acknowledged that in some cases sequence information may be held in a confidential manner by GenBank upon request by the submitter. However, it is noted that the policy of GenBank has been that *if a paper citing* the sequence *or accession number* is published prior to a specified date, the sequence *will be released upon publication*. Thus is appears that the disclosure of the GenBank accession number in Ishikawa et al. was sufficient to place the public in possession of the instantly claimed invention because even though the release date of Accession No. AB014553 was after the effective filing date of the instant claims, the policy of GenBank regarding sequence availability after publication permitted a public in possession of the Accession No. taught by Ishikawa et al. to obtain the sequence information.

It is further noted that the Ishikawa et al. indicate in Section 2.2 that the reaction conditions and PCR primers were available upon request (see especially first partial paragraph, page 172). Thus even in the absence of the GenBank accession number, it would appear that Ishikawa et al. provided the necessary information to place the public in possession of a method of making the instantly claimed invention.

Applicant is again reminded that no more of the reference is required than that it sets forth the substance of the invention. The instant limitations would be inherent properties of the protein product of KIAA0653.

The reference teachings thus anticipate the instant claimed invention.

The rejection is therefore maintained as applied to the amended claims.

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 19-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ishikawa et al (DNA Res. June 1998; 5:169-176, of record, see entire document) as evidenced by GenBank Accession No. AB014553 (released 06 Feb 1999, of record) in view of Linsley et al. (U.S. Pat. No. 5,580,756, of record).

Applicant's arguments, filed 4/30/03, with respect to the amended claims have been fully considered but have not been found convincing.

Applicant argues that Ishikawa et al. is a non-enabling reference for the reasons set forth supra, and that Linsley et al. do not remedy the deficiencies of Ishikawa et al. Applicant's arguments regarding Ishikawa et al. have not been found convincing for the reasons et forth supra.

The rejection of record is applied to the amended and newly added claims as set forth below.

The claims are drawn to compositions comprising a B7-RP1 polypeptide, derivatives of said polypeptide that include polypeptides modified with a water-soluble polymer, and fusion polypeptides comprising a B7-RP1 polypeptide.

Ishikawa et al. have been discussed supra, and in brief, teach a B7 (CD80)-related polypeptide encoded by KIAA0653.

Ishikawa et al. do not teach derivatives of said polypeptide that include polypeptides modified with a water-soluble polymer, and fusion proteins comprising the encoded polypeptide. Ishikawa et al. also do not teach formulation of the polypeptide in a pharmaceutically acceptable carrier, adjuvant, stabilizer or anti-oxidant.

Linsley et al. teach the B7 (CD80) polypeptide and its characterization as a co-stimulatory protein (see entire document, e.g., "Summary of the Invention" at columns 3-4).

Linsley et al. teach formulation of the B7 polypeptide in pharmaceutically acceptable carriers (e.g. column 12, especially lines 27-37); and the production of derivatives of the B7 polypeptide (e.g., column 6, especially lines 31-45). Although derivitization of the B7 polypeptide with a water soluble polymer was not explicitly taught by Linsley et al., modification of polypeptides with water soluble polymers such as PEG was well known in the art at the time the invention was made and in common use to improve the solubility and half-life of the polypeptide of interest.

Further, Linsley et al. teach the production of fusion proteins of the B7 (CD80) polypeptide, including fusion proteins wherein the heterologous sequence is an IgG constant domain or fragment thereof (see entire document, but especially columns 26-31). Linsley et al. also teach the application of B7Ig fusion protein for characterization of the B7 protein's co-stimulatory effect on T cells and for detecting expression of the counter receptor for B7 (see entire document, but especially columns 29-36).

Given the identification of the polypeptide of Ishikawa as a CD80 (B7)-related polypeptide, the ordinary artisan at the time the invention was made would have found it obvious to make compositions comprising the polypeptide of Ishikawa, derivatives of said polypeptide that include polypeptides modified with a water-soluble polymer, and fusion polypeptides comprising the polypeptide of Ishikawa et al. and an IgG constant domain or portion thereof. The ordinary artisan at the time the invention was made would have been motivated to produce fusion proteins comprising the B7-related protein of Ishikawa in order to further characterize the B7-related protein, and in order to identify cell types expressing the counter-receptor of this B7-related protein. Given the detailed teaching of Linsley et al. regarding production of fusion proteins comprising a B7 polypeptide, including fusion proteins of the IgG constant domain or fragments thereof, and the teachings of the amino acid and cDNA sequence by Ishikawa et al.; the ordinary artisan at the time the invention was made would have had a reasonable expectation of successfully producing the instantly recited fusion proteins. Similarly, the ordinary artisan at the time the invention was made would have been motivated to covalently modify the polypeptide with a water soluble polymer such as PEG using techniques well-known in the art at the time the invention was made in order to improve the solubility characteristics and half-life of the polypeptide. Finally, the ordinary artisan at the time the invention was made would have been motivated to formulate the polypeptide or derivative or fusion protein thereof in a pharmaceutically acceptable carrier in order to assay the activity of the polypeptide in vitro and in vivo. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

IDS

13. Applicant's IDS, filed 2/6/03 (Paper No. 20), is acknowledged.

Applicant's submission of Search Reports on the IDS is acknowledged, however this citation has been crossed out as the Search Report per se is not appropriate for an IDS.

Conclusion

14. Claims 50, 51 and 55 appear to be allowable.

15. Claims 44 and 48 would appear to be allowable if rewritten or amended to overcome the rejection under 35 U.S.C. 112, second paragraph, set forth in this Office action.

16. A claim drawn to an isolated polypeptide consisting of SEQ ID NO:12 would appear to be free of the prior art.

17. Claims drawn to an isolated polypeptide consisting of or comprising the amino acid sequence set forth in SEQ ID NO:7 would appear to be free of the prior art.

18. Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jessica Roark, whose telephone number is (703) 605-1209. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Jessica Roark, Ph.D.
Patent Examiner
Technology Center 1600
July 14, 2003

PHILLIP GAMBEL, PH.D
PRIMARY EXAMINER
TECH CENTER 1600
7/14/03